

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of

Group Art Unit: 1621

Kei YOSHIDA, et al.

Examiner: Kumar Shailendra

Serial No. 10/587,990

Filed: June 6, 2007

For: AMIDE DERIVATIVES, PROCESS FOR PREPARATION THEREOF
AND USE THEREOF AS INSECTICIDE

Honorable Commissioner of Patents and Trademarks

United States Patent and Trademark Office

Washington, D. C. 20231

Sir:

DECLARATION UNDER 37 CFR 1.132

I, Hiroyuki KATSUTA, declare and state that:

1. In March 1994, I finished Master Course in agricultural chemistry, Faculty of Agriculture in the Hokkaido University.

Since April 1994, I have been an employee of MITSUI TOATSU Chemicals, Inc. I had engaged in development of the fungicide and research of synthetic process of the same in the Agrochemicals Research Center.

In 1997, MITSUI TOATSU Chemicals, Inc. has merged with Mitsui Petrochemical Industries, LTD to form MITSUI Chemicals, Inc. Since 2000, I had engaged in development

of the insecticide and research of synthetic process of the same. Since 2008, I had engaged in above-mentioned development and research as leader of Search and Synthesis of the pesticide in Agrochemicals Research Center of MITSUI Chemicals, Inc.

In 2009, MITSUI Chemicals, Inc. has merged with Sankyo Agro, Inc to form MITSUI Chemicals Agro, Inc. Even now, I engage in development of the pesticide as staff in Research & Development Division.

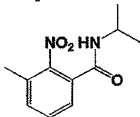
I am a co-inventor of the invention described in the above-identified application, and have a full understanding of the present invention.

2. I carried out the following experiment in order to demonstrate that when a substitution position is changed from ortho-position to meta-position in compounds described in US 6,747,047, that compound which has a substituent in meta-position can not obtained the control effects as an insecticide.

Experiment

[Comparative Example 1-1]

Preparation of N-isopropyl-3-methyl-2-nitrobenzamide



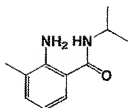
10.0g (55.2mmol) of 3-methyl-2-nitrobenzoic acid and

0.1ml of dimethylformamide were added to 50ml of toluene, and the resulting mixture was heated to 80 degree C. Then, 7.22g (60.7mmol) of thionyl chloride was dropped over 30 minutes therein, and the resulting mixture was stirred for 2 hours at 95 degree C. The reaction solution was returned to room temperature, and then the toluene was removed under a reduced pressure to obtain acid chloride as a yellow solid.

3.4g (58.0mmol) of isopropylamine and 6.1g (6.07mmol) of triethylamine were added to 50ml of THF, and the resulting mixture was cooled down to 5 degree C. The precipitated acid chloride was dissolved in 10 ml of THF, and then this THF solution was dropped over 30 minutes into the resulting mixture. The reaction solution was stirred at room temperature for 2 hour, and then the reaction solution was added in water and was extracted with ethyl acetate. The organic phase was washed with 5% hydrochloric acid and saturated sodium hydrogen carbonate, and then dried over anhydrous magnesium sulfate. The solvent was removed under a reduced pressure to precipitate a solid. The precipitated solid was washed with hexane to obtain 11.6 g of the desired product (Yield: 95%) as a light yellow solid.

[Comparative Example 1-2]

Preparation of 2-amino-N-isopropyl-3-methylbenzamide

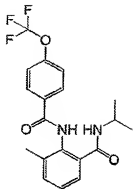


10.3g (46.3mmol) of N-isopropyl-3-methyl-2-nitrobenzamide and 5% palladium carbon were added into 70ml of methanol, and then nitrogen substitution was carried in a reaction vessel. The hydrogen was introduced, and then the resulting mixture was stirred at room temperature under normal pressures for 7 hours. The nitrogen substitution was carried, and then palladium carbon was filtered off. The solvent was removed from precipitated filtrate under a reduced pressure to obtain 9.2g of the desired product (quantitative) as a gray solid.

¹H-NMR(CDCl₃, ppm): 1.24(6H, d, J=6.7), 2.16(3H, s), 4.20-4.28(1H, m), 5.54(2H, brs), 5.85(1H, brs), 6.57-6.59(1H, m), 7.11-7.13(1H, m), 7.17-7.19(1H, m).

[Comparative Example 1-3]

Preparation of 2-(4-trifluoromethoxybenzoylamino) -N-isopropyl-3-methylbenzamide (Comparative Compound No.1)

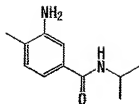


0.20g (1.04mmol) of 2-amino-N-isopropyl-3-methylbenzamide and 0.16g (2.08mmol) of pyridine were added to 5ml of ethyl acetate, and then 0.25g (1.09mmol) of 4-trifluoromethoxy-benzoylchloride was dropped therein at room temperature. The resulting mixture was stirred at 50 degree C for 2 hours. The reaction solution was returned to room temperature, and then 30 ml of ethyl acetate is added therein. The solution was washed with 5% hydrochloric acid and saturated sodium hydrogen carbonate, and then dried over anhydrous magnesium sulfate. The solvent was removed under a reduced pressure to precipitate a solid. The precipitated solid was washed with diisopropylether to obtain 0.29 g of the desired product (Yield: 74%) as a white solid.

¹H-NMR (CDCl₃, ppm): 1.18 (6H, d, J=6.6), 2.33 (3H, s), 4.10-4.17 (1H, m), 6.02-6.04 (1H, m), 7.18-7.22 (1H, m), 7.28-7.39 (4H, m), 8.03-8.07 (2H, m), 10.1 (1H, brs)

[Comparative Example 2-1]

Preparation of 3-amino-N-isopropyl-4-methylbenzamide

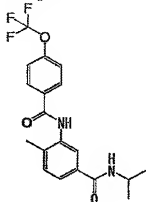


1.37g (6.62mmol) of N,N'-dicyclohexylcarbodiimide was added to 10ml of dimethylformamide, and the resulting mixture was cooled down to 5 degree C. Then, 1.01g (6.62mmol) of 1-hydroxybenzotriazole and 1.0g (6.62mmol) of 3-amino-4-methylbenzoic acid were added in order therein, and the resulting mixture was stirred for 10 minutes at 5 degree C. Then, 0.47g (7.93mmol) of isopropylamine was dropped therein, and then reaction solution was stirred for 1 hour at 5 degree C. The reaction solution was returned to room temperature, and then was stirred for 24 hours at room temperature. The reaction solution was added in water and was extracted with ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate. The solvent was removed under a reduced pressure to precipitate a residue. The precipitated residue was purified with silicagel colum chromatography (developing solvent hexane: ethyl acetate=8:2 (first), 1:1(secondly) and 2:8(thirdly)) to obtain 0.82g of the desired product (Yield: 64%) as a colorless oil.

¹H-NMR(CDCl₃, ppm): 1.23(6H, d, J=6.6), 2.19(3H, s), 3.72(2H, brs), 4.22-4.30(1H, m), 5.88(1H, brs), 6.97-6.99(1H, m), 7.06(1H, d, J=7.5), 7.13(1H, d, J=1.7)

[Comparative Example 2-2]

Preparation of N-isopropyl-4-methyl-3-(4-(trifluoromethoxy) benzamido) benzamide (Comparative Compound No.2)



0.2g (1.04mmol) of 3-amino-N-isopropyl-4-methylbenzamide and 0.16g (2.08mmol) of pyridine were added to 5ml of ethyl acetate, and then 0.25g (1.09mmol) of 4-trifluoromethoxy-benzoylchloride was dropped therein at room temperature. The resulting mixture was stirred at room temperature for 2 hours, and then 20 ml of ethyl acetate is added therein. The organic phase was washed with 5% hydrochloric acid and saturated sodium hydrogen carbonate in order, and then dried over anhydrous magnesium sulfate. The solvent was removed under a reduced pressure to precipitate a solid. The precipitated solid was washed with diisopropylether to obtain 0.35 g of the desired product (Yield: 88%) as a white solid.

$^1\text{H-NMR}$ (CDCl_3 , ppm): 1.25 (6H, d, $J=6.6$), 2.34 (3H, s), 4.22-

4.30 (1H,m), 6.01-6.03 (1H,m), 7.25 (1H,d, J=7.8), 7.34-7.37 (2H,m), 7.53-7.56 (1H,m), 7.98-8.03 (4H,m)

Test Example 1

Insecticidal Test on Common Cutworm (*Spodoptera litura*)

A piece of cabbage leaf was immersed for 30 seconds in a liquid chemical prepared by diluting a Comparative Compound to a prescribed concentration. After air-drying, the piece was put into a 7-cm polyethylene cup and second-instar larvae of common cutworms were released thereinto. The polyethylene cups were set in an isothermal chamber thermostated at 25°C. From the release 6 days later, the dead and alive were counted. The test was carried out with two replications of 5 insects per a plot.

As a result of the above test at 1000 ppm, the Comparative Compound 1 showed 100% mortality, and the Comparative Compound 2 showed 20% mortality. In addition, as a result of the above test at 100 ppm, the Comparative Compound 1 showed 100% mortality.

Test Example 2

Insecticidal Test on Diamondback Moth (*Plutella xylostella*)

A piece of cabbage leaf was immersed for 30 seconds in a liquid chemical prepared by diluting a Comparative Compound to a prescribed concentration.

After air-drying, the piece was put into a 7-cm polyethylene cup and second-instar larvae of diamondback moths were released thereinto. The polyethylene cups were set in an isothermal chamber thermostated at 25°C. From the release 6 days later, the dead and alive were counted. The test was carried out with two replications of 5 insects per a plot.

As a result of the above test at 1000 ppm, the Comparative Compound 1 showed 100% mortality, and the Comparative Compound 2 showed 0% mortality.

In addition, as a result of the above test at 100 ppm, the Comparative Compound 1 showed 100% mortality.

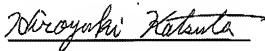
3. From the results of the above Experiment and based on my best knowledge and experience on agrochemicals, I conclude that:

It is clear that the control effect as an insecticide clearly deteriorates by only changing from ortho-position to meta-position of phenyl group as compared between Comparative Compounds No.1 and No.2.

The fact teaches clearly that a substitution position of the composition is important to improve the insecticidal activity.

The undersigned declares further that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

This 25 day of February, 2011

A handwritten signature in cursive script, reading "Hiroyuki Katsuta", written in dark ink. The signature is fluid and stylized, with the first and last names clearly legible.

Hiroyuki KATSUTA